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TECHNICAL DESIGN OF HADRON THERAPY FACILITIES

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TECHNICAL DESIGN OF HADRON THERAPY FACILITIES*

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Abstract Radiation therapy with hadron beams now has a 40-year track record at many accelerator laboratories around the world, essentially all of these originally physics-research oriented. The great promise shown for treating cancer has led the medical community to seek dedicated accelerator facilities in a hospital setting, where more rapid progress can be made in clinical research. This paper will discuss accelerator and beam characteristics relevant to hadron therapy, particularly as applied to hospital-based facilities. A survey of currently-operating and planned hadron therapy facilities will be given, with particular emphasis on Loma Linda (the first dedicated proton facility in a hospital) and HIMAC (the first dedicated heavy-ion medical facility).

RATIONALE FOR HADRONS IN RADIATION THERAPY

For almost 70 years now, radiation has been known to be effective in the treatment of cancer. In these intervening years techniques have been refined to improve cure rates and decrease the complications associated with radiation therapy. Experience has shown that treatment effectiveness is improved any time that dose to the tumor can be increased while decreasing the integrated dose to normal tissue outside the desired treatment volume. In the early days of treatment with X-ray generators, where the steep attenuation of the lower energies of X-rays available at the time ($\approx$ 250 keV) produced a much higher dose at shallow depths, it was found that dose could be concentrated in the tumor by overlapping fields brought in from many angles. With the advent of higher energy ($\approx$ 20 MeV) clinical electron accelerators the exponential attenuation of the higher-energy X-rays produced was greatly decreased, and the overlapping doses at the tumor allowed deposition of a therapeutically-effective dose with quite significant sparing of normal tissue surrounding the treatment volume. Still, many types of cancers could not be treated with X-ray beams because of the inability of these beams to avoid some critical structures in front of or behind the treatment volume.

Beams of (charged) "hadrons" (protons, helium, carbon, neon, etc. [as well as negative pi-mesons]) offer intrinsically better possibilities for precision radiotherapy, primarily because of the nature of the energy-loss mechanism for

these particles. As dE/dx ≈ 1/E, the rate of energy loss is steepest at the end of the particle range. This so-called "Bragg Peak" (Figure 1) causes deposition of a larger dose of radiation into the region where the beam is made to stop, with significantly less dose delivered to the normal tissue in front of the target, and (essentially) none to the tissue behind it. This fact was first pointed out by R.R. Wilson in 1946[1].

Hadrons, or "heavy charged particles" as they are referred to by the medical profession, have the valued characteristic that in penetrating tissue their paths, unlike those of electrons, are quite straight and so can reach tumors located deep inside a patient. However, at the required maximum depth of around 30 cm, multiple scattering and range-straggling can still be quite significant. Figure 2 shows the dose-deposition for a proton beam penetrating 25 cm into water (essentially equivalent to human tissue, for purposes of beam interactions). A beam entering with a diameter of 4 mm spreads out to over 25 mm at the stopping point. This loss of definition affects the precision possible for dose-placement with proton beams. Figure 3 compares multiple scattering and range straggling of proton beams with heavier ions. It is seen that carbon (for example) suffers about one-quarter of the beam degradation of protons, and so offers superior dose-localization potential.

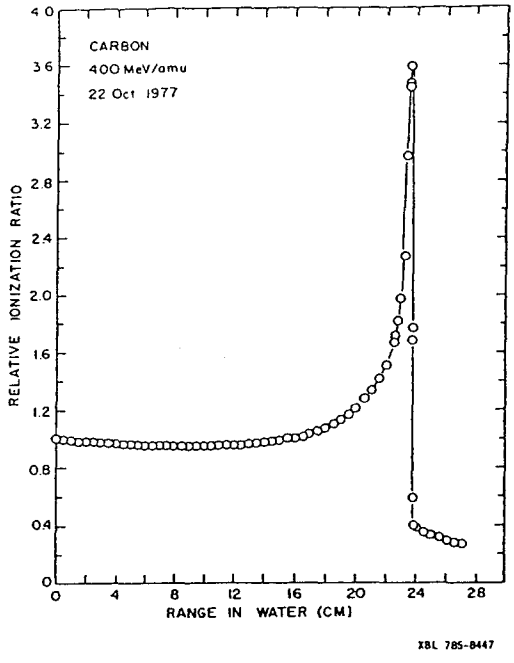

Figure 1: Bragg Peak,
dose deposition of a hadron beam

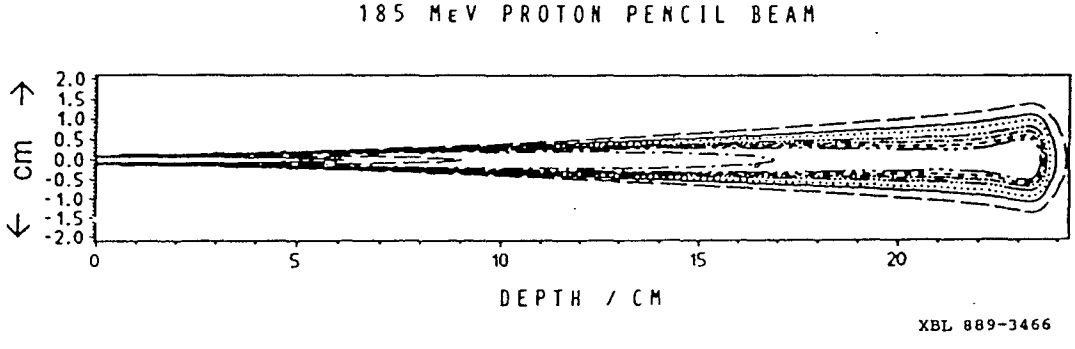

Figure 2: Proton stopping in water
spreading due to multiple scattering and range straggling
[calculation of A. Brahme, Uppsala]

Heavier ions have another characteristic that is believed to be beneficial, however clinical tests have yet to be completed. As the ionization for each particle depends on Z^2, the biological damage associated with each heavier ion will be quite a bit greater than that for a proton. This will increase the effectiveness of the ions for cell-killing in the tumor; such effects have indeed been clearly seen both in laboratory studies and in actual patient treatments. However, damage to normal tissue is also increased on the particle's path to the tumor. The response of human tissue to heavier-ion beams has been under intense study at the Bevalac in Berkeley[2], but much more work is needed to fully understand how best to use such beams for effective treatments. With the closure of the Bevalac in February 1993, and the consequent cessation of patient treatments there, this work must now wait for HIMAC, a large dedicated heavy-ion center nearing completion in Chiba, Japan[3]. This facility will be described further in a later section. A clarification regarding nomenclature: helium, carbon, and ions up through argon are referred to as either "heavy-ions" or "light-ions." In the early days of ion accelerators these were the most massive ions available, and were hence referred to as "heavy." As uranium acceleration capability became a reality, the accelerator and nuclear physics community began to make the distinction between a facility delivering all ions of the periodic table (now referred to as a "heavy-ion accelerator") calling a "light-ion accelerator" one restricted to the ions in the lower mass range. For historical and general-usage reasons, the terms are used interchangeably in this paper. Furthermore, the term "heavy-charged-particle" is used to distinguish hadrons from electrons, as therapy with electron beams is referred to by the medical community as "charged-particle" therapy.

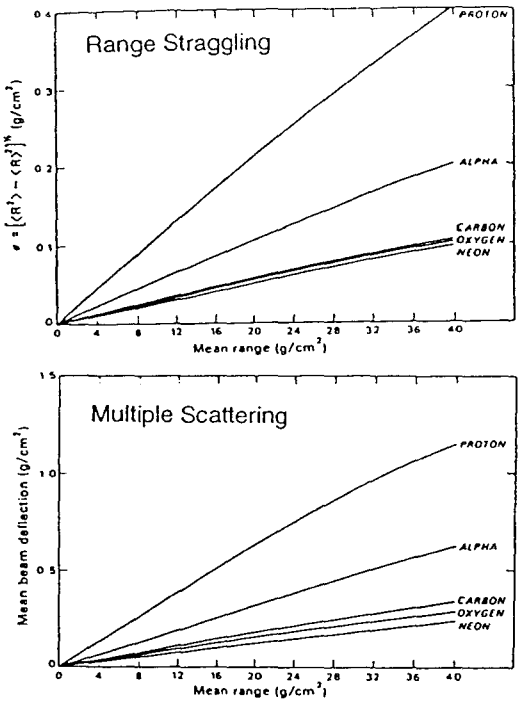

Figure 3: Range Straggling and Multiple scattering for ions
heavier ions are considerably stiffer than protons

Negative pi mesons have also been used for therapy. In addition to the increased ionization density at the stopping point (Bragg peak) of the pion, this particle is absorbed by the nucleus of the atom where it stops causing it to disintegrate with the release of a substantial amount of additional energy. This extra "star dose" adds substantially to the biological damage. Pions are harder to use, however, because of the difficulties of producing high-enough dose rates and because of the lightness of the particle (mass of the pion is only 7% that of a proton). This lower mass causes increased multiple scattering and range straggling, so the precision of placement of a pion beam is quite a bit worse than that for a proton. The fact that

pions are secondary particles makes them very expensive to produce. They require very high fluxes of protons at energies above 600 MeV to strike a production target, and a highly sophisticated transport channel to separate out the pions of the desired energy from all the contaminants produced in the target. Nevertheless, three centers around the world have treated in excess of 1000 patients with pions since 1974.

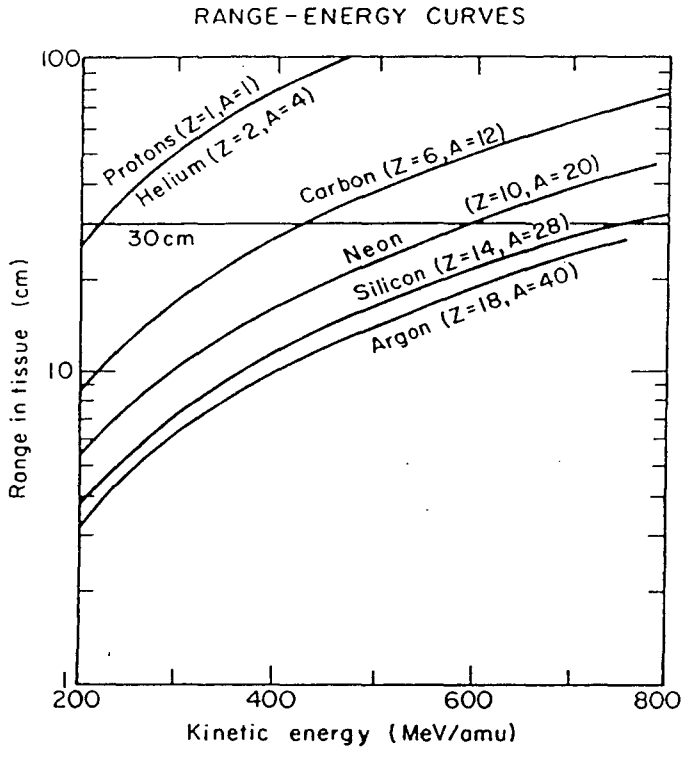

Figure 4: Range-energy curves for different ions

Although technically "hadrons," neutrons are not considered in this paper. Neutron therapy has been used since the late 1930's, its high LET (greater biological destructiveness) being used to attack radio-resistant tumors. The principal attribute of the charged hadrons discussed here is their excellent dose localization capabilities which result from their electric charge. Neutrons do not share this dose-localization property.

For several reasons clinical application of heavy charged particles is focusing on protons. First, their dose-localization ability, although not as good as for heavier ions, is still considerably better than X-rays. Second, the biological response of tissue to protons is approximately the same as that for X-rays, is very well studied and understood, so the lack of complete understanding of the dose-response of the human body associated with using heavier ions is avoided. Third, the proton beam energy needed to satisfy clinical requirements, around 250 MeV, is much lower than that needed for heavier ions. (Figure 4 shows the energy needed for different ions to penetrate a given distance in the body; for example, carbon ions must have an energy around 450 MeV/amu to penetrate 30 cm in tissue.) The magnetic rigidity ($B\rho$) for 250-MeV protons is around 2.5 Tesla-meters, while for the 450 MeV/amu carbon it is around 6 T-m. Thus a clinical accelerator for carbon ions must be about 2.5 times bigger than a similar proton accelerator. The accelerator is bigger, but more important, the gantry systems, needed for isocentric delivery, will be much bigger than the already-very-large proton gantry. (At Loma Linda, the only facility with operating gantries, the diameter of the proton gantry is 13 meters.) This point will be addressed further later on.

In summary then, although there may be some desirable features for ions heavier

than protons, size, cost, and the known biological response of protons are the determining reasons why the medical community is favoring protons as the next-generation radiotherapy modality for new hospital-based facilities.

EXPERIENCE WITH HADRON THERAPY

Hadrons have been used in therapy for 40 years now; in this time over 16,000 patients have been treated in a wide variety of radiotherapy and radiosurgery procedures. Many laboratories around the world have introduced therapy programs at accelerators whose major function is or was nuclear research. In some cases these programs operate in conjunction with ongoing nuclear research programs, in others the accelerator is dedicated to therapy applications.

The 184" synchrocyclotron at LBL was the site of the first treatments, in the early 1950's. About ten such sites have been or are being used for proton therapy, including cyclotrons at Uppsala, St. Petersburg, Dubna, Nice, Orsay, Cambridge Massachusetts, Villigen Switzerland, Chiba Japan; and synchrotrons at, Tsukuba and Moscow. Most recent addition to the synchrotron list is the facility at Loma Linda, which will be discussed at some length later in this paper. Treatments with carbon, neon, silicon and argon ions started at the Bevalac in 1975, over 400 patients received treatments with these ions through 1992. Helium ions, also considered "light ions" although resembling protons in biological effectiveness, have seen use in patient treatments also only at LBL. The 184" and the Bevalac were both used to treat over 2000 patients between 1957 and 1992. Pion treatments started at Los Alamos in 1974, and although this program stopped in 1982, work with pions is continuing at TRIUMF (Vancouver) and (until very recently) at PSI (Villigen). As stated above, over 1000 patients have been treated with negative pi-mesons. Historical summaries of the field are given by Sisterson[4] and Minakova[5].

With the exception of the Loma Linda and Nice facilities, all of the work in hadron therapy has taken place at physics research laboratories. The strong sentiment of radiotherapists working at these laboratory-based accelerators is that the environment at these sites is far from ideal for conducting a clinical program. Many difficulties are mentioned, including problems with patient access, lack of proper resources normally available in hospitals, an intimidating atmosphere for patients, and in many cases great problems in having adequate access to beam time either because of the need to share with other programs, or because the accelerator is scheduled to run only part of the year. Nevertheless, enough medical research work has been accomplished at these sites to create enthusiasm for proton therapy within the medical community. This enthusiasm has led to a strong call for building hospital-based accelerators. As mentioned above, the first of these, at Loma Linda University, is now operating, the HIMAC facility in Japan is nearing completion, and several other facilities around the world are in the planning and early design stages.

In discussions of hospital-based facilities, emphasis will be placed on requirements and specifications relevant to proton therapy. Although it is clear that some decided advantages are available with heavier beams, widespread application of these beams in a hospital setting is not likely for many years to come. The technology for hospital-based proton facilities is much more amenable for these applications in the immediate future.

SPECIFICATIONS FOR A HOSPITAL-BASED PROTON THERAPY FACILITY

The preferred beam and operational characteristics of a proton therapy facility will be discussed next, and an evaluation of available accelerator technologies will be made to determine which, if any, is most suitable for this application. As is well known, there are several different methods for producing proton beams at the desired energy, based on linear accelerator, cyclotron or synchrotron systems. However when one looks at the specific requirements for precision dose delivery, required to make best use of the excellent dose-localization properties of these particles, it becomes apparent that not all of the available technologies are equally suitable for this application.

Let us start by describing the desired specifications for a therapy beam. First of all, the beam must have enough range to reach any part of the body. The generally accepted figure is around 30 cm, leading to the 250 MeV requirement for the proton beam. (250 MeV protons actually will penetrate 38 cm in water, but the extra range is lost because of the beam-shaping and dosimetry devices the beam must pass through before reaching the patient.) Second, the beam intensity should be high enough to treat the average-sized field in about one minute. This translates into a flux of around 10^{11} protons per second that must be delivered by the accelerator. (Again, if all the particles from the accelerator could reach the treatment site, considerably less flux would be needed. To achieve the required dose distribution in the treatment field, utilization efficiency of the beam must be sacrificed; the particle-deposition rate in the target volume could be as low as 10% of the available particles.) The largest field to be irradiated is around 30 x 30 cm, and the desired uniformity of dose deposition is around ±2% across all three dimensions of the treatment field. This requires a highly-sophisticated beam delivery system, such a system is described in the next section. Then, there is a strong desire to have isocentric delivery of the beam, (keeping the patient stationary while the beam can be brought into the patient from any angle). Last but not least, the overall size and cost of the facility must be as low as possible.

The call for isocentric delivery adds significantly to the cost and complexity of the facility, but the strong justification for this capability demands its inclusion. With an isocentric gantry the patient can be treated while lying in a horizontal, supine position, and beams can be brought in to the patient from any orientation by changing the gantry angle. Less expensive is treating with a static horizontal beam, but then the patient must be immobilized in a seated or standing position. The advantages for treating a supine patient are that achieving the required immobilization is a lot easier, and most important is that diagnostic information obtained with commercial CT and MR scanners is directly applicable. Scanning a patient in the actual treatment position is essential for treatment planning and identifying anatomical coordinates for accurately directing the beam; in extreme cases organ motion of several centimeters has been observed on X-rays taken for the same patient in first a seated position then lying down.

A critical need for a clinical proton therapy system is extremely good control of the beam; its position, intensity and range must be tightly monitored and accurately controlled. This is absolutely essential for making use of the precise dose-delivery capabilities of hadron beams. The following section details reasons for this requirement.

TREATING A 3-DIMENSIONAL TARGET VOLUME

The goal is to treat an irregularly-shaped 3-dimensional target volume, conforming the areas of highest dose to this irregular shape and thus minimizing the exposure to healthy tissue outside of this volume. Achieving this is very difficult, and in fact is not being done on a routine basis for patient treatments in any of today's operating facilities. Although it is possible to shape the lateral outline of the treatment field with a complex-shaped collimator, and this is routinely done, the range modulation of the beam in all current treatments is uniform across the full treatment field. Stated differently, the volume containing stopping particles is a cylindrical section with a constant depth (z) across the entire (x,y) transverse extent of the treatment field. A "bolus compensator" is typically fabricated and placed in front of the patient to tailor the back side (distal end) of the field, but that only increases the exposure of normal tissue upstream of the target volume. This concept is illustrated in Figure 5a.

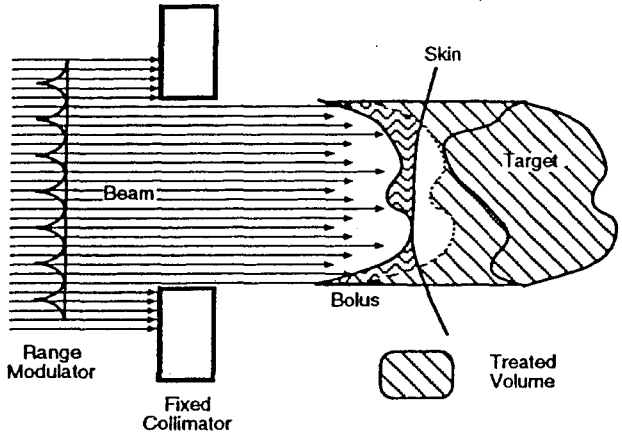

Fig 5a: 2-Dimensional Treatment System

Various schemes are being developed for achieving the goal of 3-dimensional treatments, including range-stacking with a variable collimator[6] (shown schematically in Figure 5b, described below), voxel scanning[7] and raster scanning[6], and it is anticipated that within the next five years this technology will be in actual clinical use. All of these schemes, however, require highly-accurate control over beam parameters.

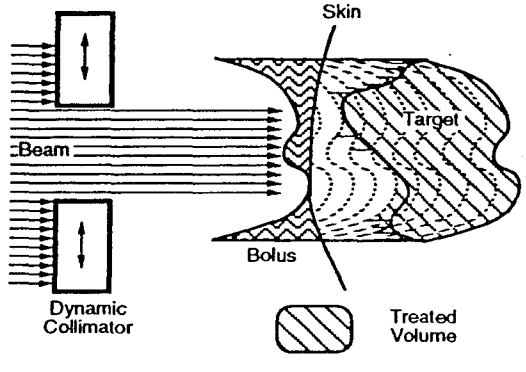

Fig 5b: 3-Dimensional Treatment System, conforming to shape of target volume

The range-stacking technique illustrated in Figure 5b has a bolus molded to allow an incident mono-energetic beam to reach the distal surface of the treatment field. The multi-leaf ("dynamic") collimator outlines the {x,y} contour of the field. The beam energy is modulated slightly, to spread the (most biologically-effective) stopping point of beam particles over a few millimeters of depth around the distal edge of the field. This volume slice is treated to the desired dose. Then, the beam energy is decreased to bring the stopping particles to the untreated volume just upstream. The multileaf is adjusted for the new {x,y} shape,

and this volume element is treated. Note that it will require less dose, as some dose was delivered to this section while the beam was treating the downstream volume slice. This process is repeated until the entire volume is treated. It is easy to see that this process will place significantly less dose in the patient outside of the desired target area.

Lateral {x,y} beam spreading can be achieved either by "passive" means, using appropriately-shaped scattering foils[8] to create beam divergence capable of covering the entire field (thickness of the foil, T = f(x,y), this shaping of the foil is used to ensure a non-gaussian, uniform field distribution) or by the "active" magnetic scanning systems mentioned above[6,7] in which a small beam spot is swept across the field by carefully-controlled magnetic deflection systems. The "passive" technique places less demands on intensity control of the beam, as the entire field is receiving dose at the same time. For "active" systems, beam intensity control must be very tight as temporal intensity variations will translate directly into spatial field dose non-uniformity. Quality of the treatment beam is not as good for scattered ("passive") beams, edge-definition is lower, higher beam energy is needed to compensate for energy-loss in the scattering system, and a higher neutron dose is generated because of nuclear interactions in the scattering foils and the heavy collimators needed to stop the high percentage of the beam (in excess of 60%) not in the suitably-uniform treatment field. Although the "active" delivery systems require substantially more control over the beam parameters, their flexibility and higher precision of treatment delivery clearly point to these techniques as superior.

For 3-dimensional treatment delivery, the depth of penetration of the beam must be adjustable independently for each (x,y) coordinate. Regardless of how the beam is painted over the volume, this independence requires that the beam energy entering the patient must be adjusted to correspond to the desired range for each element of the treatment volume. Energy adjustment can be performed by degrading the beam upstream of the patient or by varying the energy at which the beam is extracted from the accelerator. Although simpler, degrading the beam reduces the beam quality and increases the neutron dose to the patient. On the other hand, variable energy extraction introduces complexity into the accelerator design and places a further constraint on accelerator technologies that can be used. Nevertheless, because of the flexibility and higher precision, variable energy extraction is in fact preferred.

An excellent review article of the instrumentation and techniques developed for proton and heavy-ion therapy has been prepared by Chu, Renner and Ludewigt[9], a reader interested in researching the field at further depth is encouraged to study this landmark work.

APPROPRIATE ACCELERATOR TECHNOLOGIES

Summarizing the above discussion, the relative importance of the various accelerator characteristics can be listed. Very important are: adequate intensity (above 10^{11} protons/sec), excellent control of intensity over a large dynamic range (1:100 typical) in both a macroscopic and microscopic (sub-millisecond) time scale, a long duty factor (greater than 25%), a well-developed, integrated control system with a strong emphasis on safety and reliability. Important, but not as critical as the above: energy variability (70 to 250 MeV), compactness, efficiency of beam utilization and cost (both construction and operations). These factors can be

translated into an intercomparison between linac, cyclotron and synchrotron technologies for appropriateness in this proton therapy application. The Table below summarizes this intercomparison.

Table 1: Accelerator Technology Intercomparison

	Linac	Cyclotron	Synchrotron
Intensity	+ (problem, too much)	++	+ (needs care in design)
Intensity control	+ (H^- linac, laser stripping)	++ (with axial injection)	0 (needs care in design)
Duty factor	- - (very poor)	++	++
Controls	0	+	0
Safety, reliability	-	+	+
Energy variability	- (in discrete steps)	- -	++ (proton) + (H^-)
Compactness	- -	++	+ (proton) 0 (H^-)
Efficiency of beam utilization	- -	-	+ (proton) ++ (H^-)
Cost	- -	0	0
Technological risk	- -	-	++ (proton) + (H^-)

KEY: ++ excellent; + OK; 0 average; - poor; - - very poor

Linacs are clearly the least desirable of the three. Because of the extremely high voltage levels required for acceleration (hence power dissipated in the structure), linacs are generally pulsed with a very short duty factor (typically 10^{-3} or shorter). They will produce a very short, intense burst of beam at a repetition rate from a few to possibly several thousand pulses per second. Electron linacs used for medical technology are small, compact structures and can be run at very high repetition rates, but the much larger proton linacs required for 250 MeV would waste a tremendous amount of energy and require extensive cooling to run at repetition rates over a few tens of pulses per second. Continuous beams can be generated by superconducting linacs (such as at CEBAF), however this is a technology many years away from being available for hospital use. The extremely short duty factor renders linacs essentially useless for scanning system application unless the repetition rate can be in the kilohertz range: again, practical for electrons, but not for protons with today's technology. Thus, only passive scattering systems are feasible for a low-repetition-rate linac system. Even so, intensity control can be a problem. Proton linacs today are used primarily for synchrotron injection and are optimized for high instantaneous beam currents (typically in the tens of milliamps), each pulse (of duration typically a few microseconds) containing in excess of the 10^{11} to 10^{12} protons required for an entire treatment. Reducing the beam current is necessary, but places the operating point for the linac system well outside of its optimum. High instantaneous beam current resulting from the very low duty factor also creates problems with dosimetry devices, the ionization chambers used as the dosimetry standard for all radiation therapy treatments will saturate and become

non-linear well below the intensity levels available from linacs. While decreasing the beam current is possible to keep ion chambers from saturating, the low duty factor will lengthen the treatment times, to somewhere in excess of 5 minutes per treatment. Current technology for linacs would require a structure of approximately 50 to 100 meters in length to achieve the 250 MeV of energy. While compact designs have been proposed[10] that would reduce the length by about a factor of two, this technology has not yet been demonstrated for proton acceleration. In summary, if one had a linac available, it would be feasible to use it for proton therapy, however one would not be able to utilize advanced scanning beam delivery systems. Linacs would be too limiting a technology to recommend today for a stand-alone hospital-based therapy application with protons.

Cyclotrons offer many advantages over linacs. Beams are easily made to be continuous; this 100% duty cycle is very attractive for integration of advanced beam delivery systems. Beam intensity is very good, the required current of about 10 nanoamps is well within the design range of a cyclotron (currents for typical cyclotrons are in the tens of microamps range). Intensity control, and achieving the desired dynamic range for optimum treatment control could be a problem if one must rely on controlling an internal ion source. If, however, one utilizes an external source with axial injection, excellent control over the beam current is possible. Such axial injection is routinely performed with research cyclotrons, but does add significantly to the cost and complexity of the system. The compactness and simplicity of control are strong selling points for cyclotrons. Beam dynamics and overall performance are designed into the machine from the start: it either works or it doesn't. If it doesn't there's not much one can do except rebuild the cyclotron, but if it does work properly it takes very little to keep it operating at its most efficient mode. One worrisome point is that 250 MeV cyclotrons in operation today are very large structures, typically of a separated-sector design, the much-more-compact cyclotron proposed for medical application involves a radical magnetic field design that has not yet been proven.

A major drawback of the cyclotron for application with advanced beam delivery systems is the lack of beam energy variability. It is essentially impossible to extract beam from a cyclotron at any other than the full design energy. (Although this is not true for a machine accelerating H^-, the design of a variable-energy H^- machine for the range of energies required adds a level of size and complexity that would negate all the advantages of proposing a cyclotron in the first place.) To achieve the energy modulation required for controlling the depth of penetration in the target, one must rely on degraders. These can be placed in the treatment room as a part of the beam-delivery system, or in the beam switchyard well away from the patient. In the former case, although the beam transport system is quite simple and never needs to be changed during a treatment (the beam energy is the same throughout), very significant beam quality degradation results. Multiple scattering and range straggling will affect the lateral and distal edges of the beam and offset much of the dose-distribution advantage of using protons in the first place. In addition, nuclear reactions in the degrader will produce high-energy neutrons that add undesirable background radiation to the patient. Clearly more desirable is to degrade a cyclotron beam in the transport line between the accelerator and the treatment room. In this case, magnetic optics and collimation can be used to select out the portion of the degraded beam with high-enough quality (narrow energy spread and divergence) to preserve the good dose-localization properties of protons. This will

entail throwing away a good portion of the beam; for extreme energy-reduction (going from 250 MeV to 70 MeV, for instance) almost a factor of 1000 in beam-loss will be experienced. However, the cyclotron has sufficient intensity reserve to make up for the beam loss and preserve the dose rate in the treatment room. The disadvantage of this is that the beam lost at high energy will produce a lot of background radiation and material activation, requiring extensive additional shielding and presenting a long-term disposal problem of the activated material.

In the long run we believe that a positive-ion synchrotron provides the best choice as a source of 250 MeV protons for radiotherapy. The relatively large duty factors available with a well-designed slow-extraction system (typically 25 to 50%) allow for good interfacing with scanning systems and dosimetry devices. Although achieving the required beam intensity requires careful design, nonetheless such design and performance is well within the current state of the art for synchrotrons. Energy variation is very straightforward, various synchrotrons around the world have demonstrated the ability to extract beam at different flat-top fields (different energies) on subsequent pulses (examples are, SIS-18 at Darmstadt, and the CERN-PS and SPS). A medical proton synchrotron, although larger than a cyclotron, will still fit in a reasonably-sized vault (≈9 x 9 meters) and require less shielding than a cyclotron. Possible drawbacks are the increased complexity of the synchrotron system and most probably somewhat larger initial construction costs. However, with a properly-designed control system much of the tuning and operating complexity is not seen by the operator, and in fact operations and maintenance staff for the therapy facility will be comparable for both accelerators. As will be discussed in the next section, the reliability of the synchrotron system installed at the Loma Linda University Proton Facility has fully met the stringent specifications of the medical and physics staff of this hospital.

A very important consideration is flexibility and adaptability of the proton source. Because of anticipated developments in beam delivery systems, this flexibility may be a key to the ability of the proton facility to remain current in this rapidly evolving field. In this category synchrotrons have a very clear advantage over cyclotrons and linacs.

A comment is in order regarding a comparison between proton and H^- synchrotrons. Several groups are suggesting that a negative-ion machine is a better choice, however we feel that not that much is to be gained for the additional complexity associated with the use of H^-. The ring must be bigger (about twice the diameter) because Lorentz-stripping mandates a much lower magnetic field; and the vacuum system must be extremely good (10^{-10} torr or better, compared to 10^{-6} torr for protons), requiring baking and long turnaround in case of a vacuum accident. One claimed advantage is the ability to extract the beam easily with a very fine-point stripper producing a very low emittance beam. While true, this may not result in the significant reduction in the size of transport magnets claimed by the proponents. The beam aperture of the transport lines should be large enough to accommodate energy spread in the beam as well as tracking errors in beam-line tuning for rapid energy changes associated with multi-energy treatments. This aperture requirement will dominate over what would be required to transport the small emittance beam. The ability to have several extraction points around the ring may not be that much of an advantage, unless the ring is to be run at a single energy for all treatments. If variable energy treatments are to be delivered with pulses of reasonable spill-length, it is unlikely that more than one extracted beam will be in use at any one time, so a

normal switchyard would be as effective as multiple extraction points. Then also, because of the very fine extraction point, extracted beam stability may not be any better than with a resonantly-extracted beam.

LOMA LINDA UNIVERSITY MEDICAL CENTER: "LLUMPF" THE FIRST HOSPITAL-BASED PROTON THERAPY FACILITY

Located 60 kilometers east of Los Angeles, California, the Loma Linda University Medical Center has been operating the "Loma Linda University Medical Proton Facility" for proton therapy now for almost three years[11]. The facility layout, shown in Figure 6, is driven by a 250 MeV weak-focusing synchrotron designed by a Fermilab team headed by Lee Teng. A duoplasmatron source feeds a 2 MeV RFQ which single-turn injects the synchrotron. Operating at 0.5 Hz, beam is extracted over a 400 msec flattop via half-integer resonant extraction. A large switchyard sends beam to one of five irradiation areas, one fixed beam room with two ports (a dedicated eye-treatment line and a large-field station), a fixed-beam room designated as a test area, and three gantry rooms. The gantries are of the "cork-screw" design developed by Andreas Koehler of the Harvard Cyclotron Laboratory[12]. Overall gantry diameter is 13 meters, with a drift distance from the last magnet to the patient isocenter of 3 meters. The gantry design, installation and commissioning of the entire facility was performed by SAIC. Currently, beam spreading is performed using the Gottschalk-style scattering system[8], incorporated into a beam-shaping and delivery system designed with assistance from LBL. The Loma Linda facility commenced patient treatments in October 1990, and is now treating between 35 and 40 patients per day in the two rooms that have been completed. Beamlines and beam delivery systems are being installed in the remaining two gantries; these two rooms as well as the fixed-beam test-area are expected to be operational in early 1994.

Performance of the Loma Linda accelerator has been for the most part excellent, although because of design and construction deficiencies some of the original design specifications have not yet been met. The beam intensity is 2×10^{10}

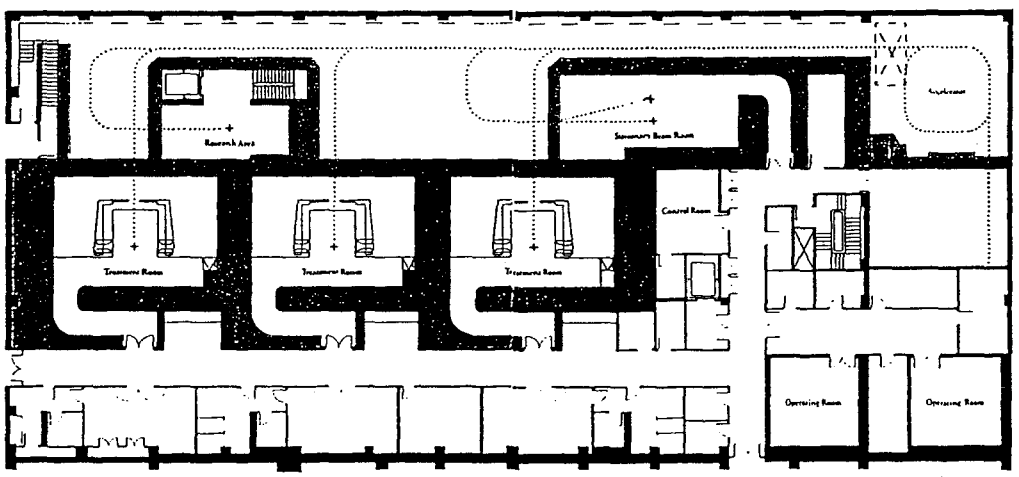

Figure 6: Layout of Loma Linda Proton Therapy Facility
Synchrotron (in upper right corner) feeds three gantry rooms and two fixed-beam rooms

protons/sec, about a factor of 5 below the original specification. Time structure of the extracted beam is very pronounced, scanning is not now possible because of inadequate control over this spill structure. The accelerator control system does not allow for rapid pulse-to-pulse energy variation, although nothing in the accelerator design prevents this from being accomplished. On the positive side, reliability, stability and operational reproducibility of the accelerator have been excellent. Upgrade efforts are now underway to correct the above-listed problems, and no impediments are seen that would prevent this facility from accomplishing all of its design and performance objectives.

NATIONAL INSTITUTE FOR RADIOLOGICAL STUDIES: "HIMAC" THE FIRST HEAVY-ION FACILITY DEVOTED TO LIFE-SCIENCES APPLICATIONS

NIRS, in Chiba, about 50 km north of Tokyo, has long been a pioneer in the use of accelerators for medical treatments. Their 70 MeV cyclotron has been used for proton and neutron treatments for well over fifteen years, and several pioneering studies in beam-delivery systems have been performed by Kawachi and his co-workers[13]. The HIMAC (Heavy Ion Medical Accelerator in Chiba) project started in 1984 and is now nearing completion, with the first patient scheduled for treatment in the spring of 1994. With basic specifications and general concepts drawn from the 1984 LBL medical accelerator design study[14], the NIRS designers selected an accelerator system capable of delivering ions of mass up to 40 (argon) at an energy of 800 MeV/amu. The layout of the HIMAC facility is shown in Fig. 7.

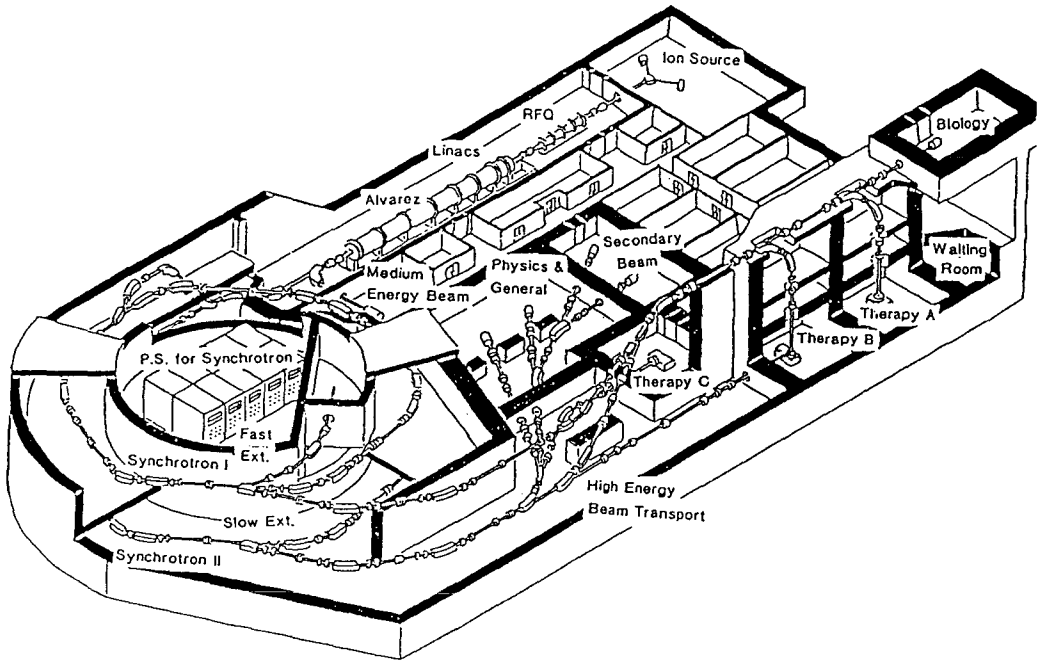

Figure 7: Layout of HIMAC facility in Chiba, Japan
Dual 800 MeV/amu synchrotrons deliver beam to three treatment rooms

Two ion sources, ECR and PIG, deliver ions from helium to argon to an RFQ followed by an Alvarez linac. Ions leave the injector system with 6 MeV/amu and are delivered to one of two identical strong-focusing synchrotrons. These over-and-under synchrotrons, separated by 10 meters in vertical elevation, add flexibility to the system: beam interchange between them is possible, as is tandem operation for added dose-rate or parallel operation in different treatment rooms. Beam is extracted over 400 msec once every two seconds and delivered to one of three treatment rooms or to biology or biophysics experimental areas. Because of the very high rigidity of the heavy-ion beams, isocentric delivery is not provided. Instead, fixed horizontal and vertical beams are brought to the treatment rooms. One room has both horizontal and vertical beams, the second a vertical only and the third a horizontal only. Beams from either ring can be delivered to any of the rooms. The beam delivery and dosimetry systems are modeled after those developed at the Bevalac: Wobbler magnets for beam spreading, range modulators and multileaf collimators for field shaping, segmented ion chambers for beam monitoring and dosimetry. This very large facility (the pit holding the building measures 60m width x 100m length x 20m depth) is now nearing completion. As of September 1993 all the accelerator and transport elements have been installed, the injection system has been operated to full specifications, first beam into the synchrotrons is expected in October, and initial studies in the treatment rooms are expected to commence in November. With the closure of the Bevalac, the mantle for continuing clinical research with heavy ions will pass to HIMAC; it is expected, with the excellent facilities being installed, that very rapid progress will indeed take place.

THE NEXT GENERATION OF HADRON-THERAPY FACILITIES

A number of initiatives are currently taking shape, that will lead to a significant increase in hadron-therapy capabilities in future years.

In Europe a new proton beam line with a novel very compact gantry and sophisticated pixel-scanning system is being built at the Paul Scherrer Institute in Villigen, Switzerland; a proton irradiation facility is being added to the COSY synchrotron facility at Jülich, Germany; plans are progressing for designing and building a therapy facility using heavy ions at GSI in Darmstadt, Germany; ITEP in conjunction with the Radiotechnical Institute in Moscow is planning an H^- synchrotron facility; and strong interest has been expressed at Clatterbridge Hospital (England), KVI (Groningen, The Netherlands) and by at least two groups in Italy for building proton-therapy facilities. These European initiatives build on the base, both technical and socio-political, that was laid by the EULIMA study concluded in 1991[15,16].

In North America proton treatments are beginning in a newly-completed treatment room at the Indiana Cyclotron facility (Bloomington, Indiana); and design studies are progressing for the NEPTC and UCCPT, proton facilities at the Massachusetts General Hospital in Boston, and the UC Davis Medical Center in Sacramento. Plans are progressing for a proton therapy room at TRIUMF to complement the pion treatments now taking place there, and centers in North Carolina and Chicago are seriously contemplating the feasibility of building proton therapy facilities. Two high-energy physics laboratories are considering the addition of proton therapy to their injector linacs: Fermilab and the SSC.

In Africa, the NAC (Cape Town) is building a proton therapy beamline to add to the neutron therapy now ongoing.

In Asia, particularly in Japan, a second light-ion facility is being proposed to be built in the Hyogo Prefecture, and proton-therapy facilities are being contemplated, in Tokyo, Tsukuba, and possibly other sites. A design for a very compact, high-field pulsed synchrotron has been developed at Novosibirsk, but at present there are no known plans for building this machine.

SUMMARY

Hadron therapy is poised for a major world-wide expansion. With the commissioning of the facility at Loma Linda, and the upcoming startup of the HIMAC facility as dedicated facilities, coupled with the many other hadron-therapy initiatives in various stages of development, this very effective therapy modality is clearly advancing rapidly. Indications are that before the end of the century possibly ten new clinical centers will be in operation or final construction stages around the world. With these added to the existing programs, developments should proceed very rapidly to fully-realize the potential of this modality for effective treatment of human cancers.

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